

What is claimed is:

1. A peptide compound comprising the formula:

R<sub>1</sub> Gln Tyr Lys Leu Gly Ser Lys Thr Gly Pro Gly Gln R<sub>2</sub> (SEQ ID NO:1),

wherein R<sub>1</sub> is absent or is an amino terminal capping group; R<sub>2</sub> is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

2. A peptide compound comprising the formula:

R<sub>1</sub> Gln Thr Leu Gln Phe Arg R<sub>2</sub> (SEQ ID NO:2),

wherein R<sub>1</sub> is absent or is an amino terminal capping group; R<sub>2</sub> is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

3. A peptide compound comprising the formula:

<sup>Asp</sup>R<sub>1</sub> <sup>Asp</sup>Xaa<sub>1</sub> <sup>Gln</sup>Gly <sup>Asp</sup>Xaa<sub>2</sub> <sup>Ala</sup>Xaa<sub>3</sub> <sup>Phe</sup>Xaa<sub>4</sub> <sup>Ala</sup>Xaa<sub>5</sub> <sup>Phe</sup>Xaa<sub>6</sub> R<sub>2</sub> (SEQ ID NO:3),

wherein R<sub>1</sub> is absent or is an amino terminal capping group of the peptide compound; Xaa<sub>1</sub> and Xaa<sub>2</sub> are, independently, aspartic acid or asparagine; Xaa<sub>3</sub> is absent or Gly; Xaa<sub>4</sub> is absent, Asp, or Phe; Xaa<sub>5</sub> is absent, Ala, or Phe; Xaa<sub>6</sub> is absent or Ala; R<sub>2</sub> is absent or is a carboxy terminal capping group of the peptide compound; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

4. The peptide compound according to Claim 3, comprising an amino acid sequence selected from the group consisting of:

Asp Gly Asp

Asp Gly Asn

Asn Gly Asn

Asn Gly Asp

~~Asp-Gly-Asp Gly Asp (SEQ ID NO:4),~~

~~Asp-Gly-Asp-Gly-Phe Ala (SEQ ID NO:5),~~

~~Asp Gly-Asp-Gly-Asp-Phe Ala (SEQ ID NO:6),~~

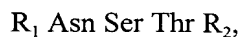
~~Asp-Gly-Asn-Gly-Asp Phe Ala (SEQ ID NO:7),~~

~~Asn-Gly Asn-Gly-Asp-Phe-Ala (SEQ ID NO:8), and~~

~~Asn Gly Asp Gly Asp Phe Ala (SEQ ID NO:9),~~

wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

5. A peptide compound comprising the formula:



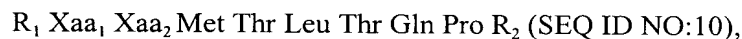
wherein  $R_1$  is absent or is an amino terminal capping group;  $R_2$  is absent or is a carboxy terminal capping; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

6. A peptide compound comprising the formula:



wherein  $R_1$  is absent or is an amino terminal capping group;  $R_2$  is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

7. A peptide compound comprising the formula:



wherein  $\text{Xaa}_1$  is absent or is Ser;  $\text{Xaa}_2$  is absent or is Lys;  $R_1$  is absent or is an amino terminal capping group;  $R_2$  is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of an antioxidative enzyme.

8. The peptide compound according to Claim 7, comprising the amino acid sequence selected from the group consisting of:



9. A peptide compound comprising the formula:

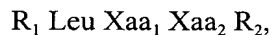


wherein  $\text{Xaa}_1$  is Asp, Asn, Glu, Gln, Thr, or Tyr;  $\text{Xaa}_2$  is absent or any amino acid;  $\text{Xaa}_3$  is Asp, Asn, Glu, Thr, Ser, Gly, or Leu;  $R_1$  is absent or is an amino terminal capping group;  $R_2$  is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

10. The peptide compound according to Claim 9, wherein Xaa<sub>2</sub> is selected from the group consisting of Val, Gly, and Glu.

11. The peptide compound according to Claim 10, wherein the peptide compound comprises the amino acid sequence selected from the group consisting of Thr Val Ser; Asp Gly Asp; Asn Gly Asn; Asp Gly; Asn Gly; Glu Gly; and Gln Gly.

12. A peptide compound comprising the formula:



wherein Xaa<sub>1</sub> is any amino acid; X<sub>2</sub> is Gln, Gly, or Tyr; R<sub>1</sub> is absent or is an amino terminal capping group; R<sub>2</sub> is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

13. A peptide compound comprising the formula:



wherein Xaa<sub>1</sub> is Asn, Asp, Gln, Glu, Thr, or Leu; R<sub>1</sub> is absent or is an amino terminal capping group; R<sub>2</sub> is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

14. The peptide compound according to Claim 13, comprising the amino acid sequence selected from the group consisting of Met Thr Leu; Met Thr Asp; Met Thr Asn; Met Thr Thr; Met Thr Glu; and Met Thr Gln.

15. The peptide compound according to Claims 1-14, wherein R<sub>1</sub> is an amino terminal capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group R<sub>3</sub>—CO—, where CO represents a carbonyl group and R<sub>3</sub> is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

16. The peptide compound according to Claim 15, wherein the amino terminal capping group is the R<sub>3</sub>—CO— acyl group wherein R<sub>3</sub> is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.

17. The peptide compound according to Claim 15, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).

18. The peptide compound according to Claims 1-14, wherein R<sub>2</sub> is the carboxy terminal capping group selected from the group consisting of a primary amine and a secondary amine.

19. A peptide compound comprising an amino acid sequence selected from the group consisting of:

~~Gln-Tyr-Lys-Leu-Gly-Ser-Lys-Thr-Gly-Pro-Gly-Gln~~ (SEQ ID NO:1);

~~Gln-Thr-Leu-Gln-Phe-Arg~~ (SEQ ID NO:2);

✓Glu Thr Leu Gln Phe Arg (SEQ ID NO:13);

✓Gln Tyr Ser Ile Gly Gly Pro Gln (SEQ ID NO:14);

✓Ser Asp Arg Ser Ala Arg Ser Tyr (SEQ ID NO:15);

~~Ser-Lys-Met-Thr-Leu-Thr-Gln-Pro~~ (SEQ ID NO:12);

~~Met-Thr-Leu-Thr-Gln-Pro~~ (SEQ ID NO:13);

~~Asp-Gly-Asp-Gly-Asp-Phe-Ala-Ile-Asp-Ala-Pro-Glu~~ (SEQ ID NO:16);

~~Asp-Gly-Asp-Gly-Asp-Phe-Ala~~ (SEQ ID NO:6);

~~Asp-Gly-Asp-Gly-Asp~~ (SEQ ID NO:4);

~~Asn-Gly-Asn-Gly-Asp-Phe-Ala~~ (SEQ ID NO:8);

~~Asn-Gly-Asn-Gly-Asp~~ (SEQ ID NO:17);

~~Asp-Gly-Asn-Gly-Asp-Phe-Ala~~ (SEQ ID NO:7);

~~Asp-Gly-Asn-Gly-Asp~~ (SEQ ID NO:18);

~~Asn-Gly-Asp-Gly-Asp-Phe-Ala~~ (SEQ ID NO:9);

~~Asn-Gly-Asp-Gly-Asp~~ (SEQ ID NO:19);

~~Asn-Gly-Asp-Gly~~ (SEQ ID NO:20);

~~Asp-Gly-Asp-Gly-Phe-Ala~~ (SEQ ID NO:5);

~~Asn-Gly-Asn-Gly-Phe-Ala~~ (SEQ ID NO:21);

~~Asp-Gly-Asn-Gly-Phe-Ala~~ (SEQ ID NO:22);

~~Asn-Gly-Asp-Gly-Phe-Ala~~ (SEQ ID NO:23);

Asp-Gly-Asp, Asn-Gly-Asn, Asp-Gly-Asn, Asn-Gly-Asp, Asn-Ser-Thr, Phe-Asp-Gln, Met Thr-Leu, Met-Thr-Asp, Met-Thr-Asn, Met-Thr-Thr, Met-Thr-Glu, Met-Thr-Gln, Thr Val Ser, Leu Thr Gln, Leu Thr Gly, Leu Thr Tyr, Asp-Gly, Asn-Gly, Glu Gly, Gln Gly, Glu Ala, Gln Ala, Gln Gly, Asp Ala, and Asn Ala,

wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

20. The peptide compound according to Claim 19, wherein the peptide compound further comprises an amino terminal capping group or a carboxy terminal capping group.

21. The peptide compound according to Claim 20, wherein the amino terminal capping group is selected from the group consisting of a reduced or oxidized lipoic acid moiety, a glucose-3-O-glycolic acid, 1-6 lysine residues, 1-6 arginine residues, an acyl group  $R_3\text{—CO—}$ , where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

22. The peptide compound according to Claim 21, wherein the amino terminal capping group is the  $R_3\text{—CO—}$  acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.

23. The peptide compound according to Claim 20, wherein the amino terminal capping group is acetyl, palmitoyl (Palm), or docosahexaenoic acid (DHA).

24. The peptide compound according to Claim 20, wherein the carboxy terminal capping group is selected from the group consisting of a primary or secondary amine.

25. A method of upregulating the level of expression of a superoxide dismutase gene, a catalase gene, or both, in cells or tissues comprising contacting cells or tissues with a peptide compound according to any one of Claims 1-24, a peptide compound comprising the formula:

$R_1$  Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu  $R_2$  (SEQ ID NO:16), or a peptide comprising the formula:

$R_1$  Glu Thr Leu Gln Phe Arg  $R_2$  (SEQ ID NO:2),

wherein  $R_1$  is absent or is an amino terminal capping group and  $R_2$  is absent or is a primary or secondary amine.

26. The method of upregulating the levels of expression of a superoxide dismutase gene, a catalase gene, or both, in cells or tissues according to Claim 25, wherein  $R_1$  is an amino terminal

capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group  $R_3$ —CO—, where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

27. The method of upregulating levels of expression of a superoxide dismutase gene, a catalase gene, or both in cells or tissues according to Claim 26, wherein the amino terminal capping group is the  $R_3$ —CO— acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.

28. The method of upregulating levels of expression of a superoxide dismutase or catalase gene, or both, in cells or tissues according to Claim 25, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).

29. A method of counteracting the oxidative effects of reactive oxygen species and free radicals in mammalian cells or tissues comprising contacting the cells or tissues with a peptide compound of any one of Claims 1-24, a peptide compound comprising the formula:

$R_1$  Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu  $R_2$  (SEQ ID NO:16), a or peptide compound comprising the formula:

$R_1$  Glu Thr Leu Gln Phe Arg  $R_2$  (SEQ ID NO:13),

wherein  $R_1$  is absent or is an amino terminal capping group and  $R_2$  is absent or is a carboxy terminal capping group.

30. The method of counteracting the oxidative effects of reactive oxygen species and free radicals in mammalian cells or tissues according to Claim 29, wherein  $R_1$  is an amino terminal capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group  $R_3$ —CO—, where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

31. The method of counteracting the oxidative effects of reactive oxygen species and free radicals in mammalian cells or tissues according to Claim 30, wherein the amino terminal capping

group is the  $R_3$ —CO— acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.

32. The method of counteracting the oxidative effects of reactive oxygen species and free radicals in mammalian cells or tissues according to Claim 30, wherein the  $R_3$ —CO— acyl group is a fatty acid.

33. The method of counteracting the oxidative effects of reactive oxygen species and free radicals in mammalian cells or tissues according to Claim 29, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).

34. The method of counteracting the oxidative effects of reactive oxygen species and free radicals in mammalian cells or tissues according to Claim 29, wherein the carboxy terminal capping group is a primary amine or a secondary amine.

35. A method of reducing or preventing an undesirable elevation in the levels of reactive oxygen species and other free radicals in cells or tissues comprising contacting the cells or tissues with a peptide compound according to any one of Claims 1-24, a peptide compound comprising the formula:

$R_1$  Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu  $R_2$  (SEQ ID NO:16), or a peptide compound comprising the formula:

$R_1$  Glu Thr Leu Gln Phe Arg  $R_2$  (SEQ ID NO:13)

where  $R_1$  is absent or is an amino terminal capping group; and  $R_2$  is absent or is a carboxy terminal capping group.

36. The method of reducing or preventing an undesirable elevation in the levels of reactive oxygen species and other free radicals in cells or tissues according to Claim 35, wherein  $R_1$  is an amino terminal capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group  $R_3$ —CO—, where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

37. The method of reducing or preventing an undesirable elevation in the levels of reactive oxygen species and other free radicals in cells or tissues according to Claim 36, wherein the amino terminal capping group is the  $R_3$ —CO— acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.
38. The method of reducing or preventing an undesirable elevation in the levels of reactive oxygen species and other free radicals in cells or tissues according to Claim 35, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).
39. The method of reducing or preventing an undesirable elevation in the levels of reactive oxygen species and other free radicals in cells or tissues according to Claim 35, wherein the carboxy terminal capping group is a primary amine or a secondary amine.
40. A method of treating or preventing a disease or condition exhibiting an undesirable elevation in levels of reactive oxygen species or other free radicals comprising administering to an individual suffering from said disease or condition a peptide compound according to Claims 1-24.
41. The method of treating or preventing a disease or condition exhibiting an undesirable elevation in levels of reactive oxygen species or other free radicals according to Claim 40, wherein the disease or condition exhibiting an undesirable elevation in levels of reactive oxygen species or other free radicals is selected from the group consisting of cerebral ischemia (stroke), myocardial infarct (heart attack), renal reperfusion damage, atherosclerosis, head trauma, brain trauma, spinal cord trauma, oxygen toxicity in premature infants, premature aging, neurodegenerative diseases, Huntington's disease, Parkinson's disease, amyotrophic lateral sclerosis, Alzheimer's disease, arthritis and other inflammatory diseases or conditions, diabetes, ulcerative colitis, human leukemia and other cancers characterized by elevation of ROS or free radicals, age-related elevation of ROS or free radicals, senility, Down syndrome, macular degeneration, cataracts, schizophrenia, epilepsy, septic shock, polytraumatous shock, burn injuries, radiation-induced elevation of ROS and free radicals, and drug-induced elevation of reactive oxygen species or other free radicals.



42. The method of treating a disease or condition exhibiting an undesirable elevation in levels of reactive oxygen species or other free radicals according to Claim 40, wherein the disease or condition is a drug-induced elevation of reactive oxygen species or other free radicals and the drug is a neuroleptic or a drug listed in Table 1.

43. The method of treating a disease or condition exhibiting an undesirable elevation in levels of reactive oxygen species or other free radicals according to Claim 42, wherein the disease or condition is Tardive dyskinesia.

44. A method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals comprising contacting cells of the mammal with a peptide compound comprising the formula:

$R_1$  Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu  $R_2$  (SEQ ID NO:16),  
wherein  $R_1$  is absent or is an amino terminal capping group; and  $R_2$  is absent or is carboxy terminal capping group.

45. The method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 44, wherein  $R_1$  is an amino terminal capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group  $R_3$ —CO—, where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

46. The method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 45, wherein the amino terminal capping group is the  $R_3$ —CO— acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.

47. The method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 44, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).

48. The method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 44, wherein the carboxy terminal capping group is a primary amine or a secondary amine.

49. The method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals according to Claims 44-48, wherein the disease or condition is selected from the group consisting of myocardial infarct (heart attack), renal reperfusion damage, atherosclerosis, head trauma, brain trauma, spinal cord trauma, oxygen toxicity in premature infants, premature aging, neurodegenerative diseases, Huntington's disease, Parkinson's disease, amyotrophic lateral sclerosis, Alzheimer's disease, arthritis and other inflammatory diseases or conditions, diabetes, ulcerative colitis, human leukemia and other cancers characterized by elevation of ROS or free radicals, age-related elevation of ROS or free radicals, senility, Down syndrome, macular degeneration, cataracts, schizophrenia, epilepsy, septic shock, polytraumatous shock, burn injuries, radiation-induced elevation of ROS and free radicals, and drug-induced elevation of ROS or free radicals.

50. The method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals according Claim 44, wherein the disease or condition is a drug-induced elevation of reactive oxygen species or other free radicals and the drug is a neuroleptic or a drug in Table 1.

51. The method of treating a disease or condition, other than stroke, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals according Claim 50, wherein the disease or condition is Tardive dyskinesia.

52. A method of treating pain in an individual comprising administering to the individual a peptide compound according to any of Claims 1-24, a peptide compound comprising the formula:

$R_1$  Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu  $R_2$  (SEQ ID NO:16), or a peptide compound comprising the formula:

$R_1$  Glu Thr Leu Gln Phe Arg  $R_2$  (SEQ ID NO:13),

wherein  $R_1$  is absent or is an amino terminal capping group; and  $R_2$  is absent or a carboxy terminal capping group.

53. The method of treating pain in an individual according to Claim 52, wherein  $R_1$  is an amino terminal capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group  $R_3$ —CO—, where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

54. The method of treating pain in an individual according to Claim 53, wherein the amino terminal capping group is the  $R_3$ —CO— acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.

55. The method of treating pain in an individual according to Claim 52, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).

56. The method of treating pain in an individual according to Claim 52, wherein the amino terminal capping group is a primary amine or a secondary amine.

57. A method of stimulating or upregulating levels of expression of an AP-1 transcription factor gene in mammalian cells comprising contacting the mammalian cells with a peptide compound of any one of Claims 1-23, or a peptide comprising the formula:



wherein  $R_1$  is absent or is an amino terminal capping group; and  $R_2$  is absent or is a carboxy terminal capping group.

58. The method of stimulating or upregulating levels of expression of an AP-1 transcription factor gene in mammalian cells according to Claim 57, wherein  $R_1$  is an amino terminal capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group  $R_3$ —CO—, where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.

59. The method of stimulating or upregulating levels of an AP-1 transcription factor gene in mammalian cells according to Claim 58, wherein the amino terminal capping group is the  $R_3$ —CO— acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.
60. The method of stimulating or upregulating levels of gene expression for AP-1 transcription factor in mammalian cells according to Claim 57, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).
61. The method of stimulating or upregulating levels of gene expression for AP-1 transcription factor in mammalian cells according to Claim 57, wherein the carboxy terminal capping group is a primary amine or a secondary amine.
62. A method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals comprising contacting cells of the mammal with a peptide compound comprising the formula:  

$$R_1 \text{ Glu Thr Leu Gln Phe Arg } R_2 \text{ (SEQ ID NO:13)}$$
 wherein  $R_1$  is absent or is an amino terminal capping group; and  $R_2$  is absent or is carboxy terminal capping group.
63. The method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 62, wherein  $R_1$  is an amino terminal capping group selected from the group consisting of a reduced or oxidized lipoic acid moiety; a glucose-3-O-glycolic acid moiety; 1-6 lysine residues; 1-6 arginine residues; an acyl group  $R_3$ —CO—, where CO represents a carbonyl group and  $R_3$  is a saturated or an unsaturated hydrocarbon chain having from 1 to 25 carbons, and combinations thereof.
64. The method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 63,

wherein the amino terminal capping group is the  $R_3$ —CO— acyl group wherein  $R_3$  is a saturated or unsaturated hydrocarbon chain having 1 to 22 carbons.

65. The method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 62, wherein the amino terminal capping group is acetyl, palmitic acid (Palm), or docosahexaenoic acid (DHA).

66. The method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or other free radicals according to Claim 62, wherein the carboxy terminal capping group is a primary amine or a secondary amine.

67. The method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals according to Claims 62-66, wherein the disease or condition is selected from the group consisting of myocardial infarct (heart attack), renal reperfusion damage, head trauma, brain trauma, spinal cord trauma, oxygen toxicity in premature infants, amyotrophic lateral sclerosis, diabetes, ulcerative colitis, human leukemia and other cancers characterized by elevation of ROS or free radicals, age-related elevation of ROS or free radicals, senility, macular degeneration, cataracts, schizophrenia, epilepsy, septic shock, polytraumatous shock, burn injuries, radiation-induced elevation of ROS and free radicals, and drug-induced elevation of ROS or free radicals.

68. The method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals according Claim 62, wherein the disease or condition is a drug-induced elevation of reactive oxygen species or other free radicals and the drug is a neuroleptic or a drug in Table 1.

69. The method of treating a disease or condition, other than stroke, Huntington's disease, Parkinson's disease, and Alzheimer's disease, in a mammal in which there is an undesirable elevation in the levels of reactive oxygen species or free radicals according Claim 68, wherein the disease or condition is Tardive dyskinesia.

70. A dietary supplement composition comprising:  
a natural source purified composition obtained from an organism comprising an endogenous peptide compound, wherein said endogenous peptide compound upregulates at least one gene encoding an antioxidative enzyme.

71. The dietary supplement composition according to Claim 70, wherein the gene encoding an antioxidative enzyme is selected from the group consisting of a gene encoding superoxide dismutase, a gene encoding catalase, and a combination of a gene encoding superoxide dismutase and a gene encoding catalase.

72. The dietary supplement composition according to Claim 70, wherein said endogenous peptide compound comprises an amino acid sequence selected from the group consisting of:

Gln Tyr Lys Leu Gly Ser Lys Thr Gly Pro Gly Gln (SEQ ID NO:1),  
Gln Thr Leu Gln Phe Arg (SEQ ID NO:2),  
Glu Thr Leu Gln Phe Arg (SEQ ID NO:13),  
Gln Tyr Ser Ile Gly Gly Pro Gln (SEQ ID NO:14),  
Ser Asp Arg Ser Ala Arg Ser Tyr (SEQ ID NO:15),  
Ser Lys Met Thr Leu Thr Gln Pro (SEQ ID NO:12),  
Met Thr Leu Thr Gln Pro (SEQ ID NO:13),  
Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu (SEQ ID NO:16),  
Asp Gly Asp Gly Asp Phe Ala (SEQ ID NO:6),  
Asp Gly Asp Gly Asp (SEQ ID NO:4),  
Asn Gly Asn Gly Asp Phe Ala (SEQ ID NO:8),  
Asn Gly Asn Gly Asp (SEQ ID NO:17),  
Asp Gly Asn Gly Asp Phe Ala (SEQ ID NO:7),  
Asp Gly Asn Gly Asp (SEQ ID NO:18),  
Asn Gly Asp Gly Asp Phe Ala (SEQ ID NO:9),  
Asn Gly Asp Gly Asp (SEQ ID NO:19),

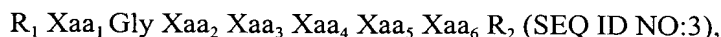
Asn Gly Asp Gly (SEQ ID NO:20),  
 Asp Gly Asp Gly Phe Ala (SEQ ID NO:5),  
 Asn Gly Asn Gly Phe Ala (SEQ ID NO:21),  
 Asp Gly Asn Gly Phe Ala (SEQ ID NO:22),  
 Asn Gly Asp Gly Phe Ala (SEQ ID NO:23),  
 Asp Gly Asp, Asn Gly Asn, Asp Gly Asn, Asn Gly Asp, Asn Ser Thr, Phe Asp Gln, Met  
 Thr Leu, Met Thr Asp, Met Thr Asn, Met Thr Thr, Met Thr Glu, Met Thr Gln, Thr Val  
 Ser, Leu Thr Gln, Leu Thr Gly, Leu Thr Tyr, Asp Gly, Asn Gly, Glu Gly, Gln Gly, Glu  
 Ala, Gln Ala, Gln Gly, Asp Ala, and Asn Ala.

73. The dietary supplement composition according to Claim 70, further comprising:  
 an exogenously provided peptide compound, wherein said exogenously provided  
 compound upregulates at least one gene encoding an antioxidative enzyme.
74. The dietary supplement composition according to Claim 73, wherein said endogenous  
 peptide compound and said exogenously provided peptide compound are the same or different  
 peptide compound that upregulates at least one gene encoding an antioxidative enzyme.
75. The dietary supplement composition according to Claim 73, wherein said endogenous  
 peptide compound and said exogenously provided peptide compound upregulate the same or  
 different gene encoding an antioxidative enzyme selected from the group consisting of a gene  
 encoding superoxide dismutase, a gene encoding catalase, and a combination of a gene encoding  
 superoxide dismutase and a gene encoding catalase.
76. The dietary supplement composition according to Claims 70 or 73, wherein said natural  
 source is green velvet antler and said organism is a ruminant.
77. The dietary supplement composition according to Claim 76, wherein said ruminant is a  
 deer or elk.
78. The dietary supplement composition according to Claims 70 or 73, wherein said organism  
 is a plant or a microorganism.

79. The dietary supplement composition according to Claim 78, wherein said plant is tea or herb.

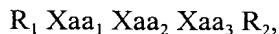
80. The dietary supplement composition according to Claim 78, wherein said natural source purified composition is wuzi yanzong herbal mixture.

81. The dietary supplement composition according to Claim 73, wherein said endogenous peptide compound and said exogenously provided peptide compound comprise, independently, a peptide compound comprising the formula:



wherein  $R_1$  is absent or is an amino terminal capping group of the peptide compound;  $\text{Xaa}_1$  and  $\text{Xaa}_2$  are, independently, aspartic acid or asparagine;  $\text{Xaa}_3$  is absent or Gly;  $\text{Xaa}_4$  is absent, Asp, or Phe;  $\text{Xaa}_5$  is absent, Ala, or Phe;  $\text{Xaa}_6$  is absent or Ala;  $R_2$  is absent or is a carboxy terminal capping group of the peptide compound; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

82. The dietary supplement composition according to Claim 73, wherein said endogenous peptide compound and said exogenously provided peptide compound comprise, independently, a peptide compound comprising the formula:



wherein  $\text{Xaa}_1$  is Asp, Asn, Glu, Gln, Thr, or Tyr;  $\text{Xaa}_2$  is absent or any amino acid;  $\text{Xaa}_3$  is Asp, Asn, Glu, Thr, Ser, Gly, or Leu;  $R_1$  is absent or is an amino terminal capping group;  $R_2$  is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

83. The dietary supplement composition according to Claim 73, wherein said endogenous peptide compound and said exogenously provided peptide compound comprise, independently, an amino acid sequence selected from the group consisting of:

Gln Tyr Lys Leu Gly Ser Lys Thr Gly Pro Gly Gln (SEQ ID NO:1),

Gln Thr Leu Gln Phe Arg (SEQ ID NO:2),

Glu Thr Leu Gln Phe Arg (SEQ ID NO:13),

Gln Tyr Ser Ile Gly Gly Pro Gln (SEQ ID NO:14),

Ser Asp Arg Ser Ala Arg Ser Tyr (SEQ ID NO:15),



Ser Lys Met Thr Leu Thr Gln Pro (SEQ ID NO:12),  
 Met Thr Leu Thr Gln Pro (SEQ ID NO:13),  
 Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu (SEQ ID NO:16),  
 Asp Gly Asp Gly Asp Phe Ala (SEQ ID NO:6),  
 Asp Gly Asp Gly Asp (SEQ ID NO:4),  
 Asn Gly Asn Gly Asp Phe Ala (SEQ ID NO:8),  
 Asn Gly Asn Gly Asp (SEQ ID NO:17),  
 Asp Gly Asn Gly Asp Phe Ala (SEQ ID NO:7),  
 Asp Gly Asn Gly Asp (SEQ ID NO:18),  
 Asn Gly Asp Gly Asp Phe Ala (SEQ ID NO:9),  
 Asn Gly Asp Gly Asp (SEQ ID NO:19),  
 Asn Gly Asp Gly (SEQ ID NO:20),  
 Asp Gly Asp Gly Phe Ala (SEQ ID NO:5),  
 Asn Gly Asn Gly Phe Ala (SEQ ID NO:21),  
 Asp Gly Asn Gly Phe Ala (SEQ ID NO:22),  
 Asn Gly Asp Gly Phe Ala (SEQ ID NO:23),  
 Asp Gly Asp, Asn Gly Asn, Asp Gly Asn, Asn Gly Asp, Asn Ser Thr, Phe Asp Gln, Met  
 Thr Leu, Met Thr Asp, Met Thr Asn, Met Thr Thr, Met Thr Glu, Met Thr Gln, Thr Val  
 Ser, Leu Thr Gln, Leu Thr Gly, Leu Thr Tyr, Asp Gly, Asn Gly, Glu Gly, Gln Gly, Glu  
 Ala, Gln Ala, Gln Gly, Asp Ala, and Asn Ala.

84. The dietary supplement composition according to any one of Claims 73-83, wherein said exogenously provided peptide compound comprises an amino terminal capping group and/or a carboxy terminal capping group.

85. The dietary supplement composition according to Claim 84, wherein the amino terminal capping group is selected from the group consisting of:

1 to 6 lysine residues; 1 to 6 arginine residues; a glucose-3-O-glycolic acid group; an acyl group containing a hydrocarbon chain from 1 to 25 carbon atoms in length; an acetyl group; a palmitoyl group; a lipoic acid group; a docosaheptaenoic acid group; and combinations thereof.

86. The dietary supplement composition according to Claim 84, wherein said carboxy terminal capping group is an amino group linked to the carboxy terminal carbonyl in an amide linkage.

87. The dietary supplement composition according to Claim 86, wherein said amino group is a primary or secondary amine.

88. A method of making a dietary supplement composition comprising:  
purifying a composition from a natural source obtained from an organism comprising an endogenous peptide compound, wherein said endogenous compound upregulates expression of at least one gene encoding an antioxidative enzyme.

89. The method of making a dietary supplement composition according to Claim 88, wherein said endogenous peptide compound comprises an amino acid sequence selected from the group consisting of:

Gln Tyr Lys Leu Gly Ser Lys Thr Gly Pro Gly Gln (SEQ ID NO:1),  
Gln Thr Leu Gln Phe Arg (SEQ ID NO:2),  
Glu Thr Leu Gln Phe Arg (SEQ ID NO:13),  
Gln Tyr Ser Ile Gly Gly Pro Gln (SEQ ID NO:14),  
Ser Asp Arg Ser Ala Arg Ser Tyr (SEQ ID NO:15),  
Ser Lys Met Thr Leu Thr Gln Pro (SEQ ID NO:12),  
Met Thr Leu Thr Gln Pro (SEQ ID NO:13),  
Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu (SEQ ID NO:16),  
Asp Gly Asp Gly Asp Phe Ala (SEQ ID NO:6),  
Asp Gly Asp Gly Asp (SEQ ID NO:4),  
Asn Gly Asn Gly Asp Phe Ala (SEQ ID NO:8),  
Asn Gly Asn Gly Asp (SEQ ID NO:17),  
Asp Gly Asn Gly Asp Phe Ala (SEQ ID NO:7),  
Asp Gly Asn Gly Asp (SEQ ID NO:18),  
Asn Gly Asp Gly Asp Phe Ala (SEQ ID NO:9),  
Asn Gly Asp Gly Asp (SEQ ID NO:19),  
Asn Gly Asp Gly (SEQ ID NO:20),  
Asp Gly Asp Gly Phe Ala (SEQ ID NO:5),  
Asn Gly Asn Gly Phe Ala (SEQ ID NO:21),

Asp Gly Asn Gly Phe Ala (SEQ ID NO:22),

Asn Gly Asp Gly Phe Ala (SEQ ID NO:23),

Asp Gly Asp, Asn Gly Asn, Asp Gly Asn, Asn Gly Asp, Asn Ser Thr, Phe Asp Gln, Met Thr Leu, Met Thr Asp, Met Thr Asn, Met Thr Thr, Met Thr Glu, Met Thr Gln, Thr Val Ser, Leu Thr Gln, Leu Thr Gly, Leu Thr Tyr, Asp Gly, Asn Gly, Glu Gly, Gln Gly, Glu Ala, Gln Ala, Gln Gly, Asp Ala, and Asn Ala.

90. The method of making a dietary supplement composition according to Claim 88, further comprising the step of:

combining said natural source purified composition with an exogenously provided peptide compound, wherein said exogenously provided compound upregulates expression of at least one gene encoding an antioxidative enzyme to form the dietary supplement composition.

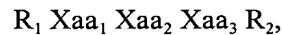
91. The method of making a dietary supplement composition according to Claim 90, wherein said endogenous peptide compound and said exogenously provided peptide compound are the same or different peptide compound.

92. The method of making a dietary supplement composition according to Claim 90, wherein said endogenous peptide compound and said exogenously provided peptide compound comprise, independently, a peptide compound comprising the formula:

$$R_1 \text{ Xaa}_1 \text{ Gly Xaa}_2 \text{ Xaa}_3 \text{ Xaa}_4 \text{ Xaa}_5 \text{ Xaa}_6 \text{ R}_2 \text{ (SEQ ID NO:3),}$$

wherein  $R_1$  is absent or is an amino terminal capping group of the peptide compound;  $\text{Xaa}_1$  and  $\text{Xaa}_2$  are, independently, aspartic acid or asparagine;  $\text{Xaa}_3$  is absent or Gly;  $\text{Xaa}_4$  is absent, Asp, or Phe;  $\text{Xaa}_5$  is absent, Ala, or Phe;  $\text{Xaa}_6$  is absent or Ala;  $R_2$  is absent or is a carboxy terminal capping group of the peptide compound; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

93. The method of making a dietary supplement composition according to Claim 90, wherein said endogenous peptide compound and said exogenously provided peptide compound comprise, independently, a peptide compound comprising the formula:



wherein Xaa<sub>1</sub> is Asp, Asn, Glu, Gln, Thr, or Tyr; Xaa<sub>2</sub> is absent or any amino acid; Xaa<sub>3</sub> is Asp, Asn, Glu, Thr, Ser, Gly, or Leu; R<sub>1</sub> is absent or is an amino terminal capping group; R<sub>2</sub> is absent or is a carboxy terminal capping group; and wherein the peptide compound upregulates expression of a gene encoding an antioxidative enzyme.

94. The method of making a dietary supplement composition according to Claim 90, wherein said endogenous peptide compound and said exogenously provided peptide compound comprise, independently, an amino acid sequence selected from the group consisting of:

Gln Tyr Lys Leu Gly Ser Lys Thr Gly Pro Gly Gln (SEQ ID NO:1),  
 Gln Thr Leu Gln Phe Arg (SEQ ID NO:2),  
 Glu Thr Leu Gln Phe Arg (SEQ ID NO:13),  
 Gln Tyr Ser Ile Gly Gly Pro Gln (SEQ ID NO:14),  
 Ser Asp Arg Ser Ala Arg Ser Tyr (SEQ ID NO:15),  
 Ser Lys Met Thr Leu Thr Gln Pro (SEQ ID NO:12),  
 Met Thr Leu Thr Gln Pro (SEQ ID NO:13),  
 Asp Gly Asp Gly Asp Phe Ala Ile Asp Ala Pro Glu (SEQ ID NO:16),  
 Asp Gly Asp Gly Asp Phe Ala (SEQ ID NO:6),  
 Asp Gly Asp Gly Asp (SEQ ID NO:4),  
 Asn Gly Asn Gly Asp Phe Ala (SEQ ID NO:8),  
 Asn Gly Asn Gly Asp (SEQ ID NO:17),  
 Asp Gly Asn Gly Asp Phe Ala (SEQ ID NO:7),  
 Asp Gly Asn Gly Asp (SEQ ID NO:18),  
 Asn Gly Asp Gly Asp Phe Ala (SEQ ID NO:9),  
 Asn Gly Asp Gly Asp (SEQ ID NO:19),  
 Asn Gly Asp Gly (SEQ ID NO:20),  
 Asp Gly Asp Gly Phe Ala (SEQ ID NO:5),  
 Asn Gly Asn Gly Phe Ala (SEQ ID NO:21),  
 Asp Gly Asn Gly Phe Ala (SEQ ID NO:22),  
 Asn Gly Asp Gly Phe Ala (SEQ ID NO:23),

Asp Gly Asp, Asn Gly Asn, Asp Gly Asn, Asn Gly Asp, Asn Ser Thr, Phe Asp Gln, Met Thr Leu, Met Thr Asp, Met Thr Asn, Met Thr Thr, Met Thr Glu, Met Thr Gln, Thr Val Ser, Leu Thr Gln, Leu Thr Gly, Leu Thr Tyr, Asp Gly, Asn Gly, Glu Gly, Gln Gly, Glu Ala, Gln Ala, Gln Gly, Asp Ala, and Asn Ala.

95. The method of making a dietary supplement according to any one of Claims 90-94, wherein the exogenously provided peptide compound comprises an amino terminal capping group and/or a carboxy terminal capping group.

96. The method of making a dietary supplement composition according to Claim 95, wherein the amino terminal capping group is selected from the group consisting of:

1 to 6 lysine residues; 1 to 6 arginine residues; a glucose-3-O-glycolic acid group; an acyl group containing a hydrocarbon chain from 1 to 25 carbon atoms in length; an acetyl group; a palmitoyl group; a lipoic acid group; a docosahexaenoic acid group; and combinations thereof.

97. The method of making a dietary supplement composition according to Claim 95, wherein said carboxy terminal capping group is an amino group linked to the carboxy terminal carbonyl in an amide linkage.

98. The method of making a dietary supplement composition according to Claim 97, wherein said amino group is a primary or secondary amine.

99. The method of making a dietary supplement composition according to Claims 88 or 90, wherein the gene encoding an antioxidative enzyme is selected from the group consisting of a gene encoding superoxide dismutase, a gene encoding catalase, and a combination of a gene encoding superoxide dismutase and a gene encoding catalase.

100. The method of making a dietary supplement according to Claims 88 or 90, wherein said natural source is green velvet antler and said organism is a ruminant.

101. The method of making a dietary supplement according to Claim 100, wherein said ruminant is a deer or elk.

102. The method of making a dietary supplement according to Claims 88 or 90, wherein said organism is selected from the group consisting of plants and microorganisms.

103. The method of making a dietary supplement according to Claim 102, wherein said natural source is wuzi yanzong herbal mixture.